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SAFETY OF CHEMICAL SMOG SUPPRESSOR

FINAL TECHNICAL REPORT
August 1977

U.S. ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF TOXIC SUBSTANCES
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It is agreed by all concerned that prior to any experimental use of these chemicals that a thorough evaluation must be made of their safety. This refers to long-term chronic effects to the environment or to persons likely to be exposed and to acute effects from exposure from credible accidents in handling and use of these chemicals.

The test protocols and the information obtained from models described in this paper should provide adequate information needed to evaluate the safety of these chemicals for the uses proposed.

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Further information can be obtained by contacting Arthur M. Stern, Chemical Testing Function, Office of Toxic Substances, Environmental Protection Agency.

SAFETY OF CHEMICAL SMOG SUPPRESSORS

Introduction

Proposals have been made to use chemicals for delaying the formation of photochemical smog. The scientific basis for this is their ability to react with and remove the free hydroxyl radical that provides the essential link in the photochemical smog chain reaction.

Diethyl hydroxylamine has been proposed by Heicklen as being particularly useful in suppressing photochemical smog (1,3).

Questions pertaining to the merit and safety of using chemicals as smog suppressors in urban environments have been raised by scientists in and out of government. The purpose of this paper is to critically review these conflicting claims and counter-claims for the benefits and risks of these proposed uses for chemicals (2).

Any serious plans for employing chemicals as smog suppressors would require evaluation of their advantages in terms of effectiveness, safety of use and economics compared to the present approach for reduction of pollutants at their emission source. The benefits to be derived by the source reduction of pollutants from mobile and stationary emissions include abatement of photochemical smog and alleviating other adverse effects from atmospheric pollutants. Adding another chemical, however, to control photochemical smog will have no effect on lowering the level of the hydrocarbons, nitrogen oxides, carbon monoxide, sulfur oxides or any of the other pollutants in our urban atmospheres.

It is not the purpose of this paper to assess the merits of various alternative approaches to reducing the adverse effects of photochemical smog by using chemicals but rather to suggest test protocols that, if adequately performed should yield the data and information needed to evaluate their merits in terms of effectiveness and safety.

Requirements for information outlined in this paper stem from proposals to release quantities of smog-suppressing chemicals into the atmosphere of our major cities where photochemical smog occurs. These urban areas have heterogenous populations that can be assumed to represent a wide range of individual sensitivities and responses to biologically active compounds present in the environment. This becomes particularly important in view of recent estimates by epidemiologists that up to 90% of the cancers reported in the U.S. are caused by environmental factors.

Chemistry

The hydroxyl radical has been found to be the critical link in the formation of photochemical smog. Several chemicals have the ability to scavenge off the free hydroxyl radical. Among these are aniline, phenol, benzaldehyde, naphthalene and diethyl hydroxylamine. All have an easily extractable hydrogen with no hydrogen associated with the alpha-carbon atom. This hydrogen combines with the hydroxyl radical to form water, thus inhibiting the photochemical reaction and the formation of oxidants. If this delay is sufficiently long--then it has been hypothesized that natural dispersive forces will dilute or remove the pollutants and also reduce the sunlight hours available. This combined effect provides a mechanism for preventing the oxidants formed in urban atmosphere form reaching problem levels that originate primarily from auto emissions (1,2,3).

Unfortunately, this chemical approach to suppressing photochemical smog will not reduce the level of hydrocarbons, nitrogen oxides or carbon monoxide in the urban atmosphere. If these pollutants are not reduced at the emission source they will continue to further build-up the potential adverse effects.

Controlling precursors of photochemical smog at the emission source is intended to provide more permanent benefits. Adding a chemical to those already present in urban atmoshperes would at best have only a cosmetic effect without reducing the total atmospheric pollutant load.

Proposed Techniques for Releasing Photochemical Smog Suppressors

Possible means for releasing suppressants to urban atmospheres are:

- Evaporation from elevated pots placed at intervals along heavily used highways.
- Spraying chemicals vertically from moving automobiles.
- Spraying from aircraft, rockets, balloons.

There is a concern on the part of government scientists and others regarding the effectiveness and safety of these chemicals when applied by these methods.

Means for dispensing chemicals need to be developed so they are uniformly dispersed at an optimal rate and the concentration maintained over the entire region to be treated during sunlight hours.

Perhaps the major logistics problem is in dispensing chemicals into the polluted urban atmosphere instantly and uniformly. Non-uniform dispersion presents several problems.

In order to assure the presence of the requisite concentration of chemicals to scavenge the free radicals, it would be necessary to use more chemicals than theoretically needed to accomplish the objectives. Also, the concentrations at the dispensing sites would, for a period of time, be much higher than the optimal level needed at reaction sites with an attendant increase in the likelihood of excessive exposure to motorists. Exposure of occupants in buildings down-wind would be also a matter of concern.

In cities such as Los Angeles there may be up to 150 days per year that could be treated with smog suppressing chemicals. If used this frequently the possibility exists that these chemicals or their derivatives might deposit on surfaces of vehicles, buildings or roads. There is also a potential run-off or wash-off from soil and surfaces or from the atmosphere that could contaminate streams and drinking water reservoirs. These problems are considered later in this paper under Methods for Evaluating Effects - Aquatic Organisms.

The likelihood of one or more chemical plumes from the surface or elevated dispensing pots combining to form a more concentrated plume or cloud should be considered in evaluating safety. Inversions, downdrafts, wind, and precipitation are micro-meterological factors that could result in the accumulation or coalescing within the lower atmospheres or upon surfaces.

Possible spillage of chemicals during transport, filling or handling and the consequences of resultant excessive environmental levels should also be considered. Accidents between vehicles carrying or dispensing the potentially hazardous chemicals and other unanticipated events, such as vandalism and natural disasters, may also be problems.

Spicer, et al, observed that certain free radical scavengers for inhibiting photochemical smog reactions can cause large increases in light scattering aerosols. They reported that this could result in a reduction of visibility from 17 miles to 0.3 miles when 0.4 ppm aniline was released to the atmosphere as an inhibitor. This type of information should be obtained in experimental smog chambers for each chemical proposed (2).

The extent that the chemicals deplete the upper atmospheric ozone layer with the attendant potential of short and long-term adverse health and climatic effects should be evaluated.

Before any chemical is used in field experiments involving potential environmental contamination a means for sampling and measuring its levels in air, water, soil and crops should be available. A monitoring program should be designed to obtain information on the current levels and trends of this chemical which would permit a determination to be made of the build-up in the environment and in the food chain.

An atmospheric dispersion model for chemicals need to be developed with time, concentration and location (horizontal and vertical) as variables. Parameters such as wind speed, inversions, downdrafts, and traffic density are examples of other inputs that must be factored into a mathematical model. Information and answers are needed on:

a) Time for effective release of chemicals
b) Places to release the chemicals
c) Amounts of chemicals to be release
d) Rate of release of chemicals
e) Time to discontinue release of the chemicals.

The precision for determining each of the above parameters would affect the amount of the chemical required to suppress smog. Since the inputs to this model change rapidly they must be available as needed.

The average large U.S. city has a rich supply of reactive pollutants in its atmosphere. Any additional chemicals added must anticipate possible atmospheric reactions between these atmospheric components and their effects. These may include sulfur and nitrogen compounds and aldehydes.

To date there is no convincing evidence that the toxic and carcinogenic diethylnitrosamines are formed in the polluted urban atmosphere in measureable quantities(5). The addition of a chemical such as diethylhydroxylamine in the quantities proposed would raise the possibility that diethylnitrosamines could be formed (a chemical or metabolic derivative) at night. This compound would be expected to decompose during sunlight hours, since it is photosensitive.

Photochemical reaction rates and products should be determined quantitatively using a simulated polluted atmosphere with added chemical suppressors in an experiment which exactly reproduces an atmospheric reaction that may occur in an urban atmosphere. This should provide clues and indicators of physico-chemical activity and other side effects(2).

Photochemical reactions also may occur on surfaces, such as, foliage, soil, glass, and in water. Although of less concern than atmospheric reactions any large scale use of a chemical would need to evaluate reaction products and the ultimate fate and transport after being released uncontrolled into the urban environment.

Toxicology of Photochemical Smog Suppressors

For chemicals that have a potential for mutagenic or carcinogenic activity

serious questions exist as to whether it is possible to assign a safe threshold exposure level. Evidence of mutagenic or carcinogenic activity observed in animal experiments may restrict any potential environmental use, such as in suppressing photochemical smog in populated urban environments(6).

In the following paragraphs the concerns expressed by government officials and others regarding the potential short-term and delayed toxic manifestations of chemicals released to populated areas are noted and the tests needed to make an assessment of these questions are outlined with references to more complete test protocols.

The feasibility or nonfeasibility of establishing a threshold, a tolerance level or a no-effect level for a chemical released to the environment where there is evidence of irreversible biological effects is presently under debate. Similarily there are environmental health scientists who question whether benefits should be weighed with risks in cases where the risks may involve adverse health effects to a segment of the population that may be sensitive to low-level chronic exposures(6).

Enormous resources would be required to assure that a chemical to be released to the atmosphere or any of its reactants would not result in abrupt or long-term effects to man or to the environment.

For a city with a large heterogeneous population such as Los Angeles it may be assumed that a certain percentage of the population will be sensitive and react adversely if exposed to a biologically active chemical. This sensitivity may not be easily detectable. However, the skin patch test on humans could be used to estimate the percentage of population sensitive to the epidermal exposure of diethylhydroxylamine.

Man's physiological make-up and his response to environmental stresses are highly variable. The onset of abnormalities such as cancer, chronic lung diseases, brain, kidney, and liver degeneration may be delayed or only be evident through accelerated aging or later show up in inherited characteristics. Increasing evidence indicates that environmental agents may be causitive factors for many degenerative diseases.

Irreversible Biological Effects

The most critical information to evaluate is that concerning irreversible adverse biological effects on humans. This refers primarily to mutagenesis, carcinogenesis and teratogenesis. The various possible routes of exposure, i.e., inhalation, oral ingestion and skin absorption should be simulated and evaluated in the laboratory.

Effects of acute, subacute and repeated low-level chronic exposures need to be evaluated for the chemical and any of its derivatives that may be formed in the urban environment.

The transport and fate of the chemical after discharging into the atmosphere are important considerations in evaluating toxic effects. Methods for measuring levels and trends in air, water and food must be known or developed. This includes intermediates, metabolites and degradation products. Possible synergistic effects from two or more atmospheric chemicals or other environmental stress would be a factor in establishing a margin of safety in estimating safe levels of exposure.

Indications that a chemical proposed for release in populated areas has been demonstrated to be a carcinogen, mutagen or a teratogen in animals test would be reason to remove it from further consideration. Where resources are limited

for testing the toxic nature of this chemical and its derivatives, it would be prudent to evaluate these chemicals in a manner that would be acceptable to Federal, State, and local authorities responsible for approving safety and efficency of use.

A battery of test methods have been developed by various laboratories for evaluating the mutagenic, carcinogenic and teratogenic activity of a chemical. References are provided for these protocols.

Methods for Evaluating Mutagenicity

There is evidence that chemicals known to be carcinogenic are also likely to be mutagenic (7,8,9).

The primary objective of mutagen testing is to determine whether a chemical has the potential of causing heritable alterations in the gene pool of man. Where chemicals are released uncontrolled to the populated urban environments the need to determine potential mutagenic activity becomes critical to the assessment of its safety for use. Direct methods for this determination in man do not exist. In recent years, a wide variety of in vitro mammalian systems have been developed that do provide useful information for determinig whether a chemical has mutagenic properties.

Test protocols for evaluating mutagenicity and carcinogenicity potential of chemicals have been described by various laboratories and investigators.

A similar program is being developed to test the mutagenic activity of pesticides by EPA, Office of Pesticide Programs in support of its Substitute Chemical Program (2) in vitro and in vivo procedures are being used by several laboratories including the Litton Bionetics and Stanford Research Institute to determine mutagenic potential of chemicals (1,16,20&21).

The Litton Bionetic scheme describes a series of mutagenic assay procedures for detecting mutagenic chemicals. This hierarchical or Tier Approach bioassays chemicals in a stepwise fashion beginning with the most rapid and inexpensive assays and continuing through the more time-consuming and costlier tests until a definite assessment appropriate to the compound in question has been determined. A chemical shown to have mutagenic properties in microorganisms would be eliminated from further consideration. At this in vitro test phase of the evaluation the costs in time and effort are relatively minor. Nonhierarchical approaches utilize a matrix of in vitro and in vivo tests all initiated simultaneously. The purpose of this approach is to obtain a multifacted data-base on a chemical. This is generally the recommended approach where only a single chemical is to be evaluated and there is a need for extensive test data in a short time frame. The matrix approach consists of two to five assays(1). A list of references includes contributions from scientists and laboratories in evaluating chemicals for their mutagenic characteristic are given in literature cited(7-21).

Methods for Evaluating Carcinogenicity

Man-made chemicals released to the environment make up part of the environmental agents believed to cause up to 90 percent of the cancers being reported in the U.S. The role of chemicals as a causitive agent in carcinogenesis is receiving increasing emphasis in the scientific community and Federal agencies, the National Institutes of Health (NCI), EPA and FDA.

In vivo animal bioassays are the only strigent proof of neoplastic activity of a chemical. This approach to evaluating carcinogenesis is expensive and may take 2 or 3 years of chronic exposures to obtain the information needed.

Considerable progress has been reported in recent years in developing rapid *in vitro* assays that are useful in predicting the potential of a chemical to initiate cancers in humans.

In vitro mutagenicity assays using microbial indicator cells coupled with mammalian microsomal activation system, (7,16,20) and *in vitro* malignant transformation assays using rodent cells (24,25,26) appear to meet the requirements of EPA in evaluating chemicals for carcinogenic potential.

A third series of assays using measures for the induction of unscheduled DNA synthesis in cultured humans cells, also correlates with known carcinogens (25,26).

Methods for Study of Reproductive and Teratogenic Toxicity

Of the principle irreversible biological diseases; cancer, mutants and teratomas, the latter concerning reproductive abnormalities is generally of lower priority when dealing with large populations for this proposed use of a chemical. The placental barrier, metabolism and diluting factors reduce the hazards to the developing embryo. The sensitivity of the embryo in various stages of development to toxic substances is also a factor that must be considered. The previous tests described for mutagenesis and carcinogenesis would, if positive, strongly suggest that the compound is also a teratogen.

Although of less priority in the evaluation scheme it would be essential to know whether a chemical had any effects on the reproductive systems of mammals if a decision was made for its large scale use to suppress photochemical smog in our large cities.

Teratologic studies have shown that the rat and mouse provides more consistent and reliable data than the rabbit or hamster. It should be noted, however,

that interspecies variation, in response to chemical dose and the difficulty of finding any correlation with human experience raises doubt as to the significance of teratologic tests(28,29).

The following references cover basic principles and procedure employed. They also include detailed protocols recommended for regulatory purposes by the FDA and the World Health Organization(29,30). Protocols for testing carcinogenic activity of chemicals are described in the literature cited(22-31). Test protocols for evaluating reproductive and teratogenic toxicity of one described in references(19-20).

Methods for Study of Inhalation Toxicity

Accidents involving processing, transport, storage, filling, or disposal of a chemical may result in acute levels in the breathing atmosphere of workers, motorists or others in close proximity. Also high levels may result close to a source of discharge of a chemical through evaporation or spraying from ground base sources or aircraft.

Airborne chemicals may be inhaled in either the vapor phase or as an aerosol, i.e., dust or mist. Studies designed to evaluate the potential hazard to humans must, therefore, relate to the nature of the physico-chemical forms in which the chemical exists and may be inhaled into the lungs.

Inhalation exposure is often a more difficult experimental procedure than administration by any other route. Since exposure of animals via the inhalation route is a specialized area, scientists experienced the use of inhalation chambers, vapor and aerosol dispersion, should be consulted(32-36).

Inhalation, as a route of entry, results in the potential for toxic effects at the site of entry, i.e., the lungs, as well as the same systemic toxic effects that

may occur from entry of the chemical into the body via other routes. Changes in pulmonary function may be the most sensitive measurement of effect when the chemical has its primary action on the lung itself. Systemic effects of a chemical including carcinogenic, mutagenic and teratogenic are measured by the same techniques utilized in studies with oral administration.

Acceptable protocols and methods for evaluating the effects, if any, of diethyl hydroxylamine and any other suppressor when inhaled are listed in references(32-36).

Methods of Evaluating Skin and Eye Toxicity

The accidental exposure to diethylhydroxylamine during processing, storage, transport, disposal or during the handling and use of a chemical for suppressing photochemical smog could result in an acute or subacute exposure to the skin or eyes.

Percutaneous absorption may be similar to oral ingestion or inhalation. Such contacts may also result in dermatitis from exposure to the primary irritant or delayed hypersensitivity. Several protocols for the study of acute and chronic percutaneous absorption and irritation type are available for use with a limited number of animal species. The human patch tests are available to determine the potential for skin sensitization chemical and to screen those susceptable to low level exposure. These tests should be conducted by a physician, and legal, ethical and medical aspects considered. Such tests may cause sensitization to a chemical. Acute exposures to potentailly hazardous chemicals are generally accidental. Subacute could result from exposures during spraying of the chemical from vehicles or evaporation from pots placed alongside a heavily travelled highway.

Acute eye contact studies can be made following one of several protocols; most employ the rabbit as the test animal. Acceptable protocols for evaluating toxic effects are described in the listed references (37-41).

Methods for Evaluating Effects on Aquatic Organisms

With over one-third of the days in Los Angeles having annoying levels of photochemical smog the repeated use of chemicals could result in an accumulation on roads, soil and buildings. Photochemical degradation and reactions with other chemical components in the atmosphere, i.e., SO_2, NO_2, etc.,could also result in the accumulation and run-off of the chemicals and their reaction products into aquatic systems. Contamination of drinking water, fish and shell-fish is also possible.

Estimates of amounts of chemicals that through run-off, fall-out, and ultimately reaching water resources should be evaluated. A transport model based on information available on the movement, reaction rates, fall-out rates, soil absorption and run-off must be developed.

Toxicity studies should include acute tests to determine the concentration in water which causes a defined effect on 50 percent of an exposed aquatic population in some short interval of time, typically, 48 to 96 hours. Chronic toxicity tests should include exposure to levels of an order of magnitude less than that where effects are observed in the acute exposure tests. These exposures involve the presence of the chemical over the life cycle of the organisms. This is from one stage in the life cycle to the same stage in the next generation. Various parameters, including survival growth rate, locomotor activity, behavioral changes, metabolities and reproductive effects should be observed, analysed and measured.

Toxicology studies in the aquatic environment are essential before full scale use of a chemical smog suppressor is undertaken. Several varieties organisms should be studied, i.e., daphnids, fish and shellfish, for potential toxic effects.

Laboratory studies using synthetic sea water and fresh water are described along with protocols for testing aquatic organisms in a synthetic or real marine and fresh water environments.

It should be possible to design a laboratory testing program providing information needed to evaluate the toxicity of a chemical to aquatic organisms that can be completed in one year or less.

Unfortunately, extrapolation from laboratory to field situations is not always easy. Organisms in the field are often subject to multiple environmental stresses that may involve synergistic effects. Open water sources, streams, reservoirs and coastal waters are subject to receiving run-off, rain-out, and fall-out of chemicals, both natural and man-caused.

It would be difficult to design a field study that would provide meaningful information on the effect of a chemical used as a smog suppressor upon a community of aquatic organisms, however, it is recommended that field tests of aquatic systems be conducted when laboratory tests made under controlled conditions indicate the need. This need could result from a finding of significant toxic effects at plausible environmental levels that could be predicted if the chemical is released into the environment in the manner proposed.

Protocols are available describing laboratory and field testing of the effects of chemical on aquatic organisms (42-47).

Contamination of Crops, Food and Feed

The proposed use of a chemical for suppressing photochemical smog is a potential source of contamination of edible crops that are used as food for humans and feed for domestic animals. Contamination of crops and feed stored in open fields for domestic animals would be a likely source of contamination. Produce from gardens, orchards and farms including leafy vegetable and fruit could be contaminated as the result of discharges of chemicals to the atmosphere. Concern usually would be with the repetitive chronic dosage to humans from consumption of food and feed that are consumed daily or periodically.

Contamination of foods such as lettuce, cabbage and broccoli should be considered in food exposure pathways directly to humans, while hay, oats, and grazing grass would be of concern through possible contamination of meat and milk-producing domestic animals. Added to this exposure would be possible contamination of drinking water.

Photochemical reactions of nitric oxide and nitrogen dioxide with unsatuarated hydrocarbons can produce phytotoxic peroxyacetyl nitrate (PAN). Ethylene, olefins, and aromatic compounds are precursors of PAN. The use of diethylhydroxylamine yields alcohol, as a photochemical product in a postulated atmospheric reaction. Ethylene, one of the procusors of PAN, is a likely intermediate. This possibility should be examined in experimental smog chambers (48).

Ethylene has been found to be toxic to vegetation. The demise of the cut-flower industry in Los Angeles and San Francisco was due, at least in part, to ethylene(49).

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